

IN THE SPECIFICATION:

Please delete the paragraph on page 1, lines 15-19 entitled "CROSS-REFERENCE TO RELATED APPLICATIONS".

Please insert the following paragraph on page 1, line 9:

CROSS-REFERENCE TO RELATED APPLICATIONS

The present application claims the benefit of priority under 35 U.S.C. Section 119(e) of United States Provisional Patent Application No. 60/448,266, filed February 17, 2003, which is incorporated herein by reference.

Please amend the paragraph at page 7, lines 23-25:

Figures 1A-1D show representative images obtained by microarray analyses using mRNA obtained from various stages of *Xenopus* embryos, wherein Figure 1A is the location of blocks 27, 28, 31, and 32 of the shown images of microarray analyses in Figures 1B-1D, and wherein Figures 1B-1D are images showing representative pseudo-colored microarray analysis of *Xenopus laevis* cleavage and neurulation stage embryos to identify patterns of altered gene expression. Figure 1B (Group I): cleavage stage embryos treated with phorbol 12-myristate 12-acetate (PMA) at pre-stage 4 (2 hours after fertilization) and harvested at stage 8 (5 hours after fertilization) incubating the embryos at 23 °C. Figure 1C (Group II): neurulation stage embryos treated with PMA at 21 hours after fertilization and harvested at 30 hours after fertilization incubating the embryos at 18 °C. Figure 1D (Group III):

Differential gene expression between cleavage stage (stage 8) and neurulation stage (stage 15) 1A-C are images showing representative pseudo-colored microarray analysis of *Xenopus laevis* cleavage and neurulation stage embryos treated with PMA to identify patterns of altered gene expression;

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Please amend the paragraph at page 30, lines 30-31:

9. Zhang, M. Q. Genome Res. 9:681-688 (1999)
(<http://www.genome.org/cgi/content/full/9/8/681>).

Please amend the paragraph at page 8, lines 11-13:

The term "screen" as used herein can include any device capable of screening for gene expression in an embryo. An example of such a screen includes, but is not limited to, a microarray.

Please amend the paragraph at page 15, line 28 to page 16, line 27:

The two fluorescent-labeled cDNA probe solutions (Cy3-labeled, green and Cy5-labeled, red, 750 ng each) were mixed, denatured and hybridized overnight at 50°C. The microarrays were then washed successively in 0.5X SSC/0.01% SDS, 0.05X SSC/0.01% SDS, 0.05X SSC/0.01% SDS, 70% ethanol, and 100 % ethanol at a constant temperature of 25°C. Hybridization of the probes and washing the microarrays were accomplished using a GENETAC hybridization station GeneTAC Hybridization Station (Genomic Solutions). Hybridization was performed with an initial

10-minute denaturation at 75°C, probe insertion at 65°C and hybridization stepped down from 65°C for 3 hours, 55°C for 3 hours to 50°C for 10 hours. Slides were washed on the station at varying stringencies starting at 50°C to room temperature. After hybridization, microarray images were obtained in a gray scale by scanning the chips at 532 nm (for green-tagged) or 635 nm (for red-tagged) and the gray scale images were false-colored in green and red, respectively. The pseudo-colored images were combined to produce microarray composite images. In the composite image, when equal amount of Cy-3 and Cy5-tagged probes were bound, the color of the spot is yellow. Imaging was carried out using GENETAC biochip analyzer ~~GeneTAC Biochip Analyzer~~ (Genomic Solutions) or GENEPIX GenePix 4000A scanner (Axon Instruments, Inc., Foster City, CA). The *Xenopus* chip has 1152 genes spotted in duplicate in a 9x9 patch, 32 grid (block) array. Bacteriophage lambda Q-gene spotted as a positive marker at the A1 and I1 positions (left and right corners on the bottom of each block) of the 32 patches (blocks). Spotting occurs in a mirror pattern using a middle vertical line as the axis. For the middle vertical line, spotting occurs in a mirror pattern using the middle empty spot as the axis. Representative pseudo-colored microarray grid images obtained from Group I, II and III are shown in Figure 1. The images were obtained without correction of the gray scale images to compensate for differences in labeling efficiency of Cy3 and Cy5. Group I was too green (Cy3) that can be corrected by multiplication by normalization factor (NF) higher than 1. Groups II and III were too red (Cy5) that can be corrected by NF lower than 1.

Please amend the paragraph at page 17, lines 8-29:

Quantitative analysis of the DNA microarrays was carried out using GENETAC genomic integrator GeneTAC Genomic Integrator (version 2.5) or GENEPIX GenePix pro (version 3.0) software. In the analysis, both median and mean values of each spot (pixel size, 20) were calculated. However, median values were used for analysis of the data because the median is much less likely to be influenced by a few bad readings. The method minimizes the effect of any aberrant samples that could distort the population distribution. Ratios of median were calculated for each spot by dividing the spot volume (integrated intensity minus background) of the Cy5 channel (red, 635 nm) by the spot volume of the Cy3 (green, 532 nm). Normalization factor (NF) was calculated for each experiment by two different methods: (a) using all the data points (~2,300) obtained by quantitation of the chip, and (b) using 64 landmark lambda Q-gene spots. Normalization of the ratio of median is necessary to correct for differences in labeling efficiency between probes. NF calculation from all data points assumes that total Cy5 signal is equal to total Cy3 signal. The primary advantage of using NF calculated from all data points is that a few erratic data points do not influence the outcome of the calculation. NF by landmarks assumes that total Cy5 signal of landmarks is equal to total Cy3 signal of the landmarks because the same amount of landmark mRNA is mixed with sample mRNA prior to probe production. A value higher than 1 means too much Cy3 or green and a value lower than 1 means too much Cy5 or red. Trends of NF values obtained for each experiment obtained by two different methods were in agreement.